Humanized Mice Reveal Differential Immunogenicity of Cells Derived from Autologous Induced Pluripotent Stem Cells.

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Public Summary:
The breakthrough of induced pluripotent stem cell (iPSC) technology has raised the possibility that patient-specific iPSCs may become a renewable source of autologous cells for cell therapy without the concern of immune rejection. However, the immunogenicity of autologous human iPSC (hiPSC)-derived cells is not well understood. Using a humanized mouse model (denoted Hu-mice) reconstituted with a functional human immune system, we demonstrate that most teratomas formed by autologous integration-free hiPSCs exhibit local infiltration of antigen-specific T cells and associated tissue necrosis, indicating immune rejection of certain hiPSC-derived cells. In this context, autologous hiPSC-derived smooth muscle cells (SMCs) appear to be highly immunogenic, while autologous hiPSC-derived retinal pigment epithelial (RPE) cells are immune tolerated even in non-ocular locations. This differential immunogenicity is due in part to abnormal expression of immunogenic antigens in hiPSC-derived SMCs, but not in hiPSC-derived RPEs. These findings support the feasibility of developing hiPSC-derived RPEs for treating macular degeneration.

Scientific Abstract:
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